

0908 '00 APR -7 A9:37

Atrial Fibrillation Device Therapies

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Overview

- AF Clinical Facts
- AF Device Therapies
- July 1998 Panel Meeting
- Definitions of Success
- Clinical Trial Designs
- Questions for the Panel
 - Pacemakers and Implantable Atrial Defibrillators
 - Catheter Ablation Systems

Atrial Fibrillation (AF)

- Most common chronic tachycardia
- Most common cardiac cause of stroke
- ~ 6% of US population > 60 years have AF
- Incidence increases with ↑ age
- Significant public health concern

AF Device Therapies

- Pacemakers
- Implantable Atrial Defibrillators
- Catheter Ablation Systems
 - Linear Ablation (MAZE)
 - Focal Pulmonary Vein (PV) Ablation

Previous Panel Considerations

- July 1998 - Panel made recommendations regarding AF Ablation clinical trial design
- Today - Broaden to include discussion of Pacemakers and Atrial Defibrillators

Definitions of Success

- AF Ablation - Definitions of acute and chronic success are well-characterized in medical literature.
- Pacemakers & Atrial Defibrillators - Success criteria are not as well-defined.
- What are clinically meaningful measures of device effectiveness?

Clinical Trial Designs

- Randomized - Treatment vs. Control
- Crossover - Treatment ON vs. OFF
- Baseline - Baseline Observation Period
Followed by Treatment Period

Questions for the Panel

Pacemakers and Implantable Atrial Defibrillators

Study Design

Pacemakers and Implantable Atrial Defibrillators

1. Discuss study design options below first for pacemakers, and then for implantable atrial defibrillators.

- a. Randomized Controlled Study
- b. Single-Arm Crossover Study
- c. Single-Arm Prospective Baseline Period

Study Endpoints

Pacemakers and Implantable Atrial Defibrillators

2. Discuss whether reduction in occurrence of:

- a) symptomatic, or
 - b) symptomatic + asymptomatic episodes
- would be considered clinically relevant in demonstrating effectiveness of AF pacing therapies.

Study Endpoints

Pacemakers and Implantable Atrial Defibrillators

3. How should "burden" be defined?

- a. Time spent in AF, AT, and/or AT/AF
- b. Days in which a patient has at least one AT/AF episode
- c. Other

Study Endpoints

Pacemakers and Implantable Atrial Defibrillators

4. For implantable atrial defibrillators, is atrial shock therapy effectiveness best measured by the ability to terminate AF/AT episodes?

What other endpoints do you think might be appropriate?

Success Criteria

Pacemakers and Implantable Atrial Defibrillators

5. Discuss whether your expectation for a clinically-relevant percent reduction in AF episodes would be altered by the risk-benefit profile for pacing therapy.

Catheter Ablation Systems

Catheter Ablation Systems

Study Design

1. Discuss the advantages and disadvantages of the following study designs:
 - a. Randomized Controlled Study
 - b. Single-Arm Prospective Baseline Study
 - c. Single-Arm Retrospective Baseline Study
 - d. Other

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Inclusion Criteria

2. What inclusion criteria may be reliably used to identify patients in whom AF is believed to originate in the PVs?
 - a. patients with monomorphic and/or inferiorly directed premature atrial contractions (PACs)
 - b. patients with ectopic foci mapped during electrophysiologic study to the PVs
 - c. patients with a history of paroxysmal AF
 - d. other

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Identification of Target Ablation Sites

3. If a patient is not in AF at the time of the PV ablation procedure, and if the patient is also non-inducible for AF, can you recommend what electrophysiological criteria investigators might use in identifying which PV(s) to ablate?

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Acute Success

4. Which reliable physiologic criteria might be used to evaluate the acute success of the PV ablation procedure?
- a. post-ablation non-inducibility
 - b. loss of atrial capture
 - c. decrease in atrial electrogram amplitude
 - d. measurement of "electrical isolation" of the abated PV (how would you evaluate this electrophysiological parameter?)
 - e. Other

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Success Criteria

5. In July 1998, the Circulatory System Devices Panel suggested that 50-75% reduction in frequency of AF episodes would be a clinically relevant reduction for linear ablation procedures.

Please discuss whether your expectation has changed for this endpoint, given the increased use of RF ablation as a treatment modality.

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PV Thrombosis and Pulmonary HTN

6. Recent articles in the medial literature suggest that some patients may experience pulmonary vein thrombosis as a result of the PV ablation procedure. Is there a relatively low risk (i.e., minimally invasive) method for evaluating PV thrombosis during the early post-ablation period? Patients may also develop pulmonary hypertension. Likewise, is there a relatively low risk method for evaluating pulmonary hypertension during the follow-up period?
